The prognostic value of peripheral blood inflammatory indices early variation in patients (pts) with metastatic renal cell carcinoma (mRCC) treated with nivolumab (Δ-Meet-URO analysis).

Sara Elena Rebuzzi, Alessio Signori, Sebastiano Buti, Giuseppe Luigi L. Banna, Marco Stellato, Daniele Santini, Umberto Basso, Ugo De Giorgi, Silvia Chiellino, Alessia Salfi, Paolo Andrea Zucali, Cristina Masini, Emanuele Naglieri, Giuseppe Procopio, Michele Milella, Francesco Boccardo, Lucia Fratino, Stefania Pipitone, Camillo Porta, Giuseppe Fornarini, Meet-URO: Italian Network For Research In Urologic-Oncology; Department of Internal Medicine and Medical Specialties (Di.M.I.), University of Genova, Genova; Medical Oncology Unit, Ospedale San Paolo, Savona, Italy; Department of Health Sciences (DISSAL), Section of Biostatistics, University of Genova, Genova, Italy; Medical Oncology Unit, University Hospital of Parma, Parma, Italy, Department of Medicine and Surgery, University of Parma, Parma, Italy; Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy; Department of Medical Oncology, Fondazione Policlinico Campus Bio-Medico, Roma, Italy; Medical Oncology 1 Unit, Department of Oncology, Istituto Oncologico Veneto IOV IRCCS, Padua, Italy; IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy; Medical Oncology Unit, IRCCS Policlinico San Matteo, Pavia, Italy; Medical Oncology Unit 2, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy; Department of Biomedical Sciences, Humanitas University, Pieve Emanuele; Department of Oncology, IRCCS, Humanitas Clinical and Research Center, Milano, Italy; Medical Oncology Unit, AUSL-IRCCS of Reggio Emilia, Reggio Emilia, Italy; Division of Medical Oncology, IRCCS Istituto Tumori "Giovanni Paolo II", Bari, Italy; Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; Section of Oncology, Azienda Ospedaliera Universitaria Integrata di Verona, University of Verona, Verona, Italy; Academic Unit of Medical Oncology, IRCCS Ospedale Policlinico San Martino, Genoa, Italy; Department of Medical Oncology, Centro di Riferimento Oncologico di Aviano CRO-IRCCS, Aviano, Italy; Medical Oncology Unit, Department of Oncology and Hemathology, University Hospital of Modena, Modena, Italy; Chair of Oncology, Department of Biomedical Sciences and Human Oncology, University of Bari 'A. Moro'; Division of Medical Oncology, A.O.U. Consorziale Policlinico di Bari, Bari, Italy; Medical Oncology Unit 1, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Background: Immunotherapy has improved the treatment landscape of mRCC pts and identifying biomarkers for patients' selection is clinically needed. Inflammatory indices from peripheral blood showed a prognostic value in different tumors and therapies, including immunotherapy. These biomarkers are inexpensive and readily available in clinical practice. We aimed to assess the prognostic role of the dynamic evaluation of these indices in immunotherapy-naïve pretreated mRCC pts. **Methods:** The Meet-URO 15 multicentric retrospective study enrolled 571 pretreated mRCC pts receiving nivolumab. The Δ-Meet-URO was a secondary analysis on the early variation through the first four cycles of therapy compared with baseline (difference, delta - Δ) of white blood cells, platelets and inflammatory indices, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII, platelets x NLR), their comparison with baseline values and correlation with treatment response, overall (OS) and progression-free survival (PFS). The baseline and Δ cut-offs were identified by ROC curves for OS. **Results:** The analysis was performed on 422 mRCC pts (74% of the entire cohort). Patients with ΔNeutrophils < 730 at 2nd, 3rd and 4th cycles were more responders ($p < 0.001$, $p = 0.003$ and $p < 0.001$) with longer mPFS (11 *vs* 6.1 months, $p = 0.033$) and mOS (46.9 *vs* 20.8 months, $p = 0.046$) compared to ΔNeutrophils ≥ 730. There was a significant interaction between baseline and ΔNeutrophils on PFS ($p = 0.047$). Pts with baseline neutrophils ≥ 4330/mm^3 had longer mPFS when ΔNeutrophils < 730 ($p = 0.002$), whilst no difference was observed in those pts with baseline neutrophils < 4330/mm^3 according to ΔNeutrophils ($p = 0.46$). Similar non-significant trends were observed in mOS. Patients with ΔNLR < 0.5 at 3rd and 4th cycles were more responders ($p = 0.004$ and $p = 0.001$, respectively) with doubled mPFS (12.1 vs 6.4 months, $p = 0.007$) and mOS (46.9 vs 21.7 months, $p = 0.062$) compared to ΔNLR ≥ 0.5. No significant interaction between baseline NLR and ΔNLR was observed in PFS and OS, suggesting a similar association between ΔNLR and PFS or OS, regardless of the baseline NLR cut-off of 3.2. The multivariable analyses confirmed all these results. **Conclusions:** The early assessment of NLR and neutrophils variations during immunotherapy for mRCC pts is a promising, affordable and non-invasive prognostic tool. Prospective and external validation analyses are warranted. Research Sponsor: Italian Ministry of Health (Ricerca Corrente 2018–2021 grants).